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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/629,463

07/29/2003

Frederick Hicks

RD 02038

7309

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03/27/2007

EXAMINER

LAO, MARIALOUISA

ART UNIT

PAPER NUMBER

1621

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
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3 MONTHS

03/27/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary

Application No.

10/629,463

Applicant(s)

HICKS, FREDERICK

Examiner

MLouisa Lao, Ph.D.

Art Unit

1621

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 16 January 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-22 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-22 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date 7/29/03.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of the groups in the reply filed on January 16, 2007 is acknowledged. The traversal is on the ground(s) that the application meets the unity of invention requirements as stipulated under 37 C.F.R. §1.475 and §1.499.
2. Having taken the applicants' arguments into advisement, the restriction requirement has been withdrawn and all the claims are examined in their entirety on the merits.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. **Claims 1-18 are rejected** under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a base, like potassium hydroxide and potassium carbonate, does not reasonably provide enablement for "*alkaline earth carbonate, bicarbonate, sulfonate or phosphonate*". The specification does not enable the person skilled in the art of synthetic chemistry, to make the invention commensurate in scope with these claims. The factors to be considered [in making an enablement rejection] have been summarized as a) the quantity of experimentation necessary, b) the amount of direction or guidance presented, c) the presence or absence of working examples, d) the nature of the invention, e) the state of the prior art, f) the relative skill of those in the art, g) the predictability or unpredictability of the art, and, h) the breadth of the claims.

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In the present case, the important factors leading to a conclusion of lack of scope of enablement are the absence of any working example of alkaline earth carbonate, bicarbonate, sulfonate or phosphonate, the quantity of experimentation necessary, and the broad scope of the claims.

a) the quantity of experimentation necessary. Since there are at least 6 elements in the alkaline earth metal family and four form variations (i.e. carbonate, bicarbonate, sulfonate or phosphonate) in which these could be in, the permutation of combinations and subcombinations to be tested are proportionately numerous.

b) the amount of direction or guidance presented. The instant specification in pages 14-15 provides guidance for using alkali earth metal hydroxide and carbonates (KOH and K_2CO_3), but not for alkaline earth metal salts as bases for the arylation method described in the instant claims.

c) the presence or absence of working examples. There are no working examples of alkaline earth metal carbonate, bicarbonate, sulfonate or phosphonate. The two examples, directed to potassium hydroxide and potassium carbonate, presented in pages 14-15 of the specification are found atypical of the purported nature of the base as recited in the claims; since potassium belongs to the alkali earth metals.

d) the nature of the invention. The nature of the invention falls under a general category of known chemical processes.

e) the state of the prior art. The prior art (US6335463, US'463) shows the use of alkali earth metal salts as bases in an arylation synthesis.

f) the relative skill of those in the art. The persons of ordinary skill in the art at the time of the invention would be synthetic organic chemists.

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g) the predictability or unpredictability of the art. Catalysts are unpredictable. Thus, the processes dependent thereto, would likewise proceed in an unpredictable manner; since a catalyst that is efficacious for an epoxidation process may not predictably behave the same way in a hydrogenation process.

h) the breadth of the claim. Claim 1 is broad since it encompasses the plurality of all alkaline earth carbonate, bicarbonate, sulfonate or phosphonate.

5. MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/use the full scope of the claimed invention without undue experimentation. In re Wright 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed.Cir.1993)." That conclusion is clearly justified here. Thus, undue experimentation will be required to practice Applicants' invention.

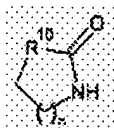
6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

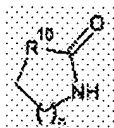
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

7. **Claims 5 and 6 are rejected** under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

8. Claim 5 recites the limitation "wherein nucleophile comprises an amide, a carbamate, a urea, or a sulfonamide" in line 1. There is insufficient antecedent basis for this limitation (a carbamate, a urea, or a sulfonamide) in the claim; since claim 4, on which claim 5 is dependent upon, also recites "*wherein nucleophile comprises a HN-containing heterocycle comprising a*

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monocyclic system according to the formula  wherein $n=0$ or $1-3$ and R^{10} =substituted alkyl, substituted N or O”.

9. **Claim 6**, which ultimately depends on claim 4, recites only one compound (N-methylimidazolidinone) that reads on the definition of a nucleophile of claim 4; whereas the rest of the compounds recited therein are atypical of a nucleophile that is an HN-containing heterocycle, since the ring structures of the compounds recited contain carbon atoms only.

Claim Rejections - 35 USC § 102/ § 103

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

12. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

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1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

13. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

14. **Claims 1, 2, 7, 8, and 19 are rejected under 35 U.S.C. 102(a) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Sommer (US6335463, US'463).**

15. The instant claims are drawn to a method of arylating a nucleophile, comprising reacting the nucleophile with a substrate aromatic compound, ArX, in the presence of a copper catalyst, a base and water, wherein Ar=aryl, heteroaryl or alkenyl; X=halo, sulfonate or phosphonate, base comprises an alkaline earth carbonate, bicarbonate, hydroxide or phosphate and the copper catalyst comprises a copper atom or ion and a ligand. Further the nucleophile comprises a HN-containing heterocycle or a HN-containing compound, described in the claims, as recited.

16. The instant claims recite potassium hydroxide or potassium carbonate as suitable bases for arylation.

17. US'463 in claims 1, 3 and 4 column 8 lines 27-59 and 63-67 and in claim 33 column 10 lines 46-48, recites a method of arylating a nucleophile, which encompasses the reaction in the

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presence of a copper catalyst, a base and water, where the nucleophile is N-(4-fluorophenyl)glycine, wherein correspondingly in the instant claims, this compound fits the HN-containing compound according to the formula $\text{HN}(\text{R}_1)\text{R}_2$, wherein $\text{R}_1 = \text{aryl}$ and $\text{R}_2 = \text{R}_3\text{-C(=O)-}$ and $\text{R}_3 = \text{-OR}_5$; and, the aromatic compound is dichlorobenzoic acid, wherein correspondingly in the instant claims, this compound fits ArX , $\text{Ar} = \text{aryl}$, phenyl ring, which is substituted, other than the X substituent in addition to the X substituent, on one or more carbons of the ring (herein, the substituents are -Cl , COOM_1) and $\text{X} = \text{halo}$. Albeit the reacting compounds are alkali metal salts, these are the same alkali metals as the base compounds (see column 9 claim 10), US'463 states that the alkali metal salt forms of the reacting compounds render a more efficacious reaction to proceed.

18. US'463 in column 5 Example 1 discloses that the copper catalyst is present at 4mole%, the ArX is at 2.1 equivalents relative to the nucleophile and in column 4 lines 38-39, the amount of water is minimally present.

19. US'463 does not disclose the base for arylation to encompass alkaline earth metal carbonate, bicarbonate, sulfonate or phosphonate.

20. However, in page 12 lines 17-20 of the instant specification, the applicants recite compounds as suitable base components, enumerating therein both alkali and alkaline earth metal salts; including examples thereto on pages 14-15 directed to alkali earth hydroxide and alkali earth carbonate. Said disclosure sets forth an equivalency between alkali earth metal salts and alkaline earth metal salts as bases that can be used in the instant claimed process.

21. It would be obvious to one skilled in the art at the time of the invention to substitute the alkali earth metal salts as bases in the US'463 method with the alkaline earth metal salts as

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disclosed in the instant application since these were stated in the instant specification to be equivalent.

22. One having ordinary skill in the art would have been motivated to use bases comprising alkaline earth metal salts in lieu of alkali earth metal salt since these are equivalent and the artisan would reach a reasonable degree of success as in the instant application.

23. Thus, US`463 renders the instant claims, as recited unpatentable.

Claim Rejections - 35 USC § 102/103

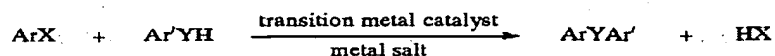
24. **Claims 1 -22 are rejected** under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Marcoux et al. (US6395939, US`939) and further in view of Zanon et al. (US2005/0101788, US`788) and Sommer (US6335463, US`463).

25. The instant claims are drawn to a method of arylating a nucleophile, comprising reacting the nucleophile with a substrate aromatic compound, ArX, in the presence of a copper catalyst, a base and water, wherein Ar=aryl, heteroaryl or alkenyl; X=halo, sulfonate or phosphonate, base comprises an alkaline earth carbonate, bicarbonate, hydroxide or phosphate and the copper catalyst comprises a copper atom or ion and a ligand. Further the nucleophile comprises a HN-containing heterocycle or a HN-containing compound, described in the claims, as recited.

26. The instant claims recite potassium hydroxide or potassium carbonate as suitable bases for arylation.

27. US`939 discloses in column 2 lines 33-58, an arylation synthesis that encompasses the reaction as shown:

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wherein

Ar and Ar' independently represent optionally substituted aryl or heteroaryl groups;

YH represents a substituent of Ar' that includes a nucleophilic group, or a group that can be rendered nucleophilic;

X represents a leaving group which can be substituted by the nucleophilic group of Y in a transition metal-catalyzed reaction;

the transition metal catalyst is a complex which catalyzes formation of ArYAr' from ArX and Ar'YH;

the metal salt has an anionic portion that is sufficiently basic to neutralize the HX produced in the reaction and/or deprotonate Ar'YH and thereby render it a better nucleophile, and the metal salt comprises a soft cation selected from the alkali metal or alkaline earth series,

wherein, correspondingly in the instant claims, the arylation takes place between the aromatic compound= ArX and the nucleophile= Ar'YH in the presence of a base and copper catalyst.

28. US'939 discloses a typical example of the reaction supra in column 19 scheme 6 lines 33-48 with the reaction of 3-bromoquinoline and N-methylaniline.

29. US'939 also discloses the typical Copper catalysts in column 23 lines 11-60, which include copper ion sources.

30. Albeit, US'939 does not expressly disclose specific substituents for ArX and Ar'YH and the copper catalyst comprising, *inter alia*, a ligand; and the use of base and water, US'788 and US'463 are relied upon to answer these deficiencies.

31. US'788 discloses in page 8 claim 1 that sertindole can be manufactured with the reaction of 5-chloroindole, which is a nucleophile and HN-containing compound, with 4-fluorophenylhalide, which is an aromatic halide, in the presence of a base, a chelating ligand and copper catalyst. In page 2 section[0021], US'788 states that the chelating agent is the compound of the formula X-(CR¹R²-(CR⁵R⁶)_n-CR³R⁴-Y)_m, which read on the ligand of instant claims 13

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and 14, when X and Y = NR₇R₈ and R₇ and R₈ are independently H, C1-6 alkyl; when n=0,1,2,3 and R₁-R₉ independently are selected from hydrogen, C1-6 alkyl, C1-6 aryl; when m=1.

32. While US'463, described in detail supra under claim rejections under 35USC 102/103, discloses the use of water in an arylation method to produce sertindole.

33. As stated supra, US'463 does not disclose the base for arylation to encompass alkaline earth metal carbonate, bicarbonate, sulfonate or phosphonate. In the same token, US'788 discloses in page 2 [0025] the use of alkali earth metals like potassium and sodium carbonates; but does not disclose alkaline earth metal carbonate, bicarbonate, sulfonate or phosphonate.

34. However, in page 12 lines 17-20 of the instant specification, the applicants recite compounds as suitable base components, enumerating therein both alkali and alkaline earth metal salts; including examples thereto on pages 14-15 directed to alkali earth hydroxide and alkali earth carbonate, in contrast to the claimed definition of a base compound in claim 1 lines 4-5, which recites "the base comprises an alkaline earth metal carbonate, bicarbonate, sulfonate or phosphonate".

35. It would have been obvious to a person of ordinary skill in the art at the time of the invention was made to employ the specific compounds, 5-chloroindole with 4-fluorophenylhalide of US'788 and the water in US'463, and the reaction parameters thereto and therewith, using the alkali earth metal salts as bases in the arylation method of US '939 since the compounds and parameters are applicable for equivalent types of arylation methods and these compounds fit the definition profiles of a nucleophilic compound and an ArX, respectively and

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the parameters (i.e. base and water and Cu catalyst), as in the parameters recited in the instant application using the equivalent alkaline earth metal salts as bases, with water and a Cu catalyst.

36. One having ordinary skill in the art would have been motivated to do combine the teachings of US`788, US`463 and US`939, since the arylation methods are essentially the same and equally employ compounds and reaction parameters that are equivalent as defined in the instant application and the artisan would have expected a reasonable degree of success.

37. Thus, the combined teachings of US`788, US`463 and US`939 render the instant claims, as recited, unpatentable.

Correspondence

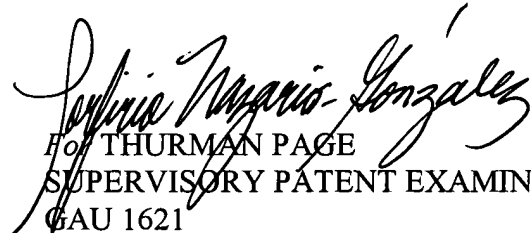
Any inquiry concerning this communication or earlier communications from the examiner should be directed to MLouisa Lao, Ph.D. whose telephone number is 571-272-9930. The examiner can normally be reached on 8:30am to 5:30pm Mondays to Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page can be reached on 571-272-0602. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

ml 02272007
MLouisa Lao, Ph.D.
Examiner
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